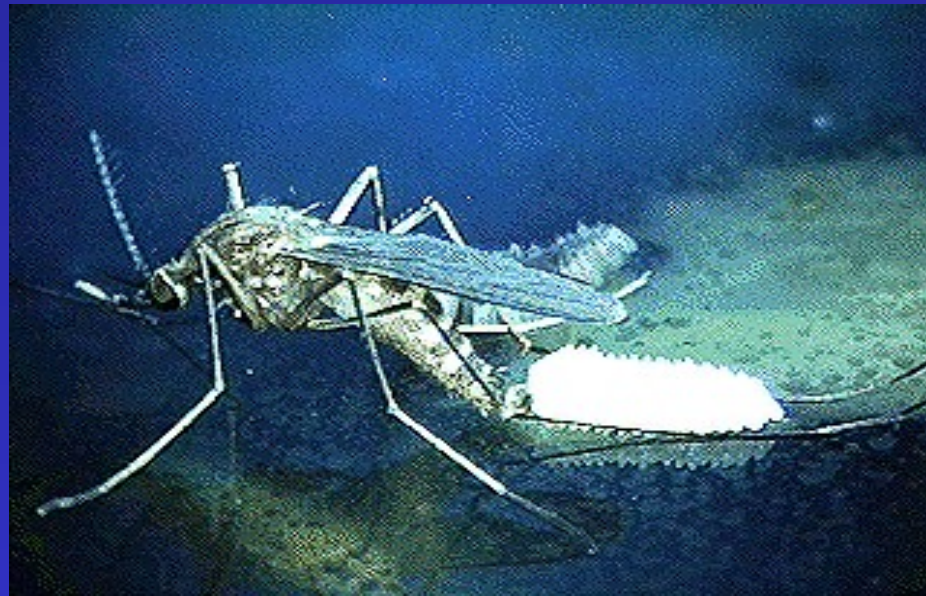


West Nile Virus and the Clinician

Bryan Fisk, MD



Case Presentation

- 25 yo WF w/o significant PMH
- C/O fever of 101 to 105F and chills for 2 days
- HA, neck soreness
- Nausea and vomiting
- Lethargy
- Slight non-productive cough
- Denies rhinorrhea, sore throat, dyspnea, abdominal pain, diarrhea, or dysuria

Case Presentation - Continued

- Patient lives in Laurel, Maryland on a wooded lot along the Patuxent river
- Reports clearing dead crow from her yard 4 days prior to admission
- Multiple mosquito bites
- Physical exam s/f mild photophobia on ocular exam, significant discomfort on neck flexion but absence of nuchal rigidity, and mild inspiratory crackles of RML field

What is the West Nile Virus?

- A Member of the Arbovirus Group (Arthropod Borne viruses)
 - Group of viruses transmitted by blood-sucking arthropods (vectors)
 - Include Alphaviruses and Flaviviruses
 - Vectors include both mosquitoes and ticks
 - Mosquitoes account for majority by far

Flavivirus Family

- Enveloped positive-sense RNA viruses
- Enveloped viruses more unstable than naked viruses: Unstable in the environment, sensitive to heat, ultraviolet radiation, disinfectants (including alcohol and iodine) and acid pH
- Lipid envelope covered with M (membrane) and E (envelope) glycoproteins

Flaviviruses (continued)

- E protein functions include:
 - Viral-cellular attachment (cellular receptor is unknown)
 - Endosomal membrane fusion
- Acid milieu of endosome results in fusion activity, nucleocapsid uncoating, and release of viral RNA into cytoplasm
- E proteins are also the sites recognized in viral neutralization
 - Important antigen for host defenses

Mode of Transmission

- Vector: Mosquitoes (mainly *Culex* species)
- Amplifying or reservoir host: wild birds
 - mainly American crows in the U.S.
 - 90% to 100% mortality rate
 - Blue jays 2nd most common
 - Flamingos in Bronx zoo
 - New research suggests large role for sparrow
- Incidental end-stage hosts: Mammals
 - Including humans and horses
 - No human-to-human spread

Geographic Location of WNV

- Endemic in Africa, the Middle East, India, and Asia
- Also found in parts of Europe and the former U.S.S.R.
- First reported in the Western hemisphere in 1999

Location of WNV in U.S.

- Originally detected in Connecticut, New York, New Jersey, and Maryland in 1999
- In 2000 - detected in CT, DE, MD, MA, NH, NJ, NY, NC, PA, RI, VT, and VA
- CDC plans to have nation-wide surveillance in 2001

Wild Bird Cases: Cumulative Report

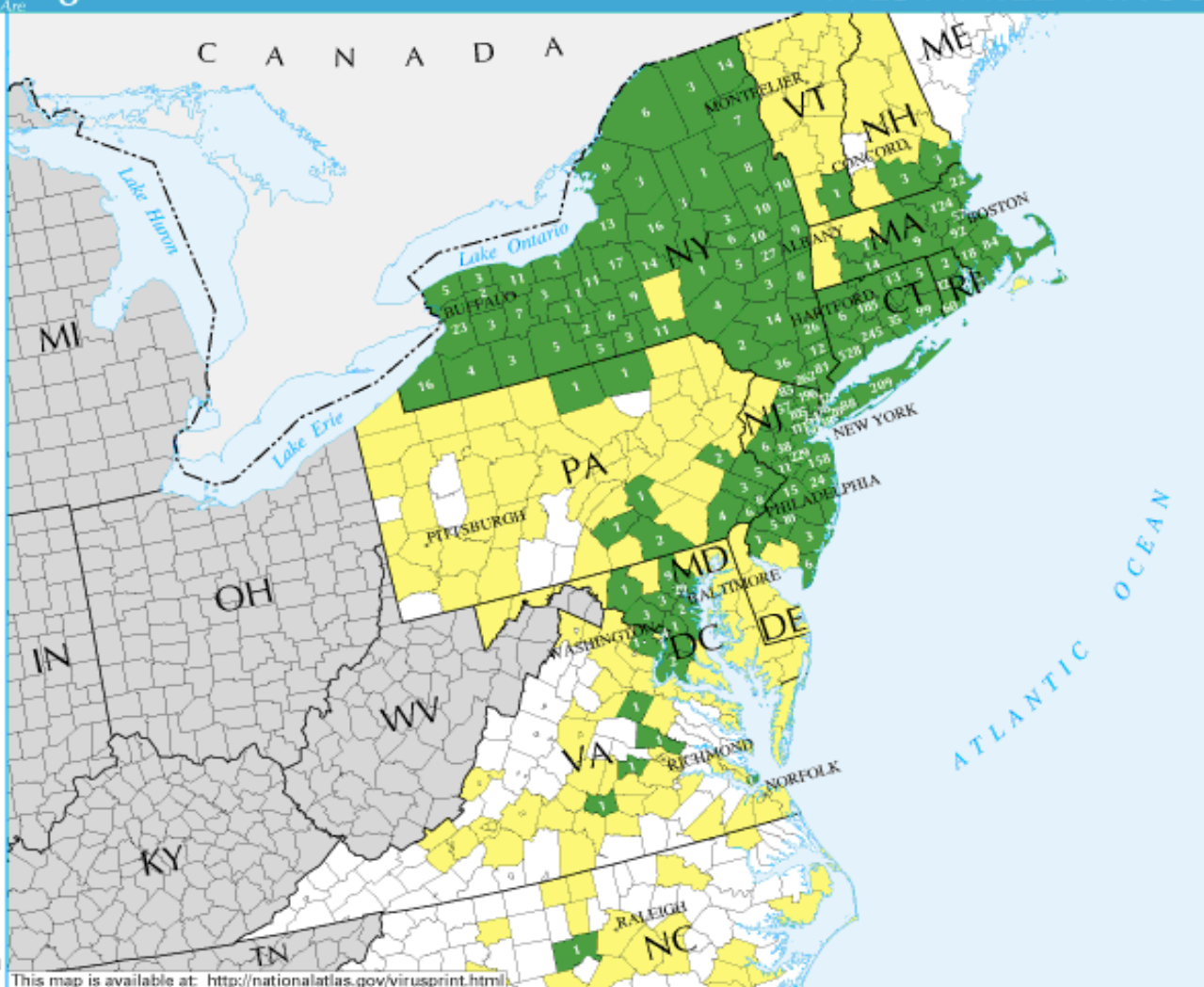
Data from reports made
between 1 JAN 00 and 10 NOV 00.

- Number of Positives
 Test Samples Submitted
 No Reports
 Not Participating

These county and county equivalent data are based on tests of tissue samples from dead and diseased wild birds, provided by state health officials. Many of these data represent crows, which are especially sensitive to West Nile virus (WNV). Note that the map includes all areas of positive (confirmed or probable) WNV results, but not necessarily all areas with submitted samples or no reports.



Disclaimer: These data are provisional and may be revised or adjusted in the future.



This map is available at: <http://nationalatlas.gov/virusprint.html>

U.S. Department of the Interior
U.S. Geological Survey

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

The National Atlas of the United States of America®

Epidemiology of West Nile Fever

- 1937 - First reported in Uganda
- 1950's - Egyptian outbreak
- 1957 - Outbreak of meningoencephalitis in Israel, affecting 400 people
- 1970's - South African outbreak
- 1996 - Romanian outbreak, approx 400 cases
- 1999 - NYC outbreak
- 2000 - Outbreak in Israel with 169 cases and 12 deaths as of September 2000

Epidemiology of West Nile Fever

- New York City epidemic – 1999
 - NYC metropolitan area epidemic of encephalitis/meningitis of an unknown etiology
 - Initially misidentified as St Louis Encephalitis
 - 66 human cases
 - 7 deaths
 - N. American WNV most closely related to WNV isolated from a dead goose in Israel in 1998
 - 18 hospitalized cases and one death in 2000

West Nile Fever

- Infection usually self-limited
 - 3 to 5 days in 80% of patients
- Human infection common in endemic areas
 - > 60% of young adults with antibodies
 - High prevalence of inapparent or undifferentiated febrile illness in children
 - This results in protected populations with life-long immunity

West Nile Fever

- Incubation period: 1 to 6 days
- Abrupt onset w/o prodromal symptoms
- Fever from 38.3 to 40C with rigor in 1/3 of patients
- Malaise/drowsiness/lethargy/fatigue
- Severe frontal HA and ocular pain

West Nile Fever

- Generalized lymphadenopathy
- Polyarthropathy
- *Roseolar maculopapular rash in 1/2 of pts*
- *Severe muscle weakness and myalgia*
- Neurologic involvement in minority

Review of Encephalitis

- Inflammation of the brain
 - Related terms are **meningitis** (inflammation of the meninges), **meningoencephalitis** (brain and meninges), and **encephalomyelitis** (brain and spinal cord)
 - Distinction between aseptic meningitis and viral encephalitis is clinical and often indistinct
- Inflammation of encephalitis may be focal, multi-focal or diffuse
 - Neurologic vs hematologic spread to CNS
- Damage results from swelling (cerebral edema), intercerebral hemorrhage, and nerve damage
 - Nerve damage from cytopathic vs immune-mediated effects

Review of Encephalitis

- Typically due to viral infections
- Herpes viruses and arboviruses are the most common causes
 - Arbovirus infections occur in the summer and fall
 - HSV-1 and Varicella-zoster encephalitides are the only effectively treatable form of encephalitis (HSV-2 more likely to cause meningitis)

Encephalitis Symptoms

- Lethargy
- Stiff neck/back
- Photophobia
- Seizures (may be see in meningitis)
- Lethargy
- Confusion
- Vomiting
- Ataxia
- Aphasia
- Tremor
- Partial paralysis
- Coma (secondary to displacement of the brain-stem)



West Nile Encephalitis

- Severe neurologic disease is the exception
 - Serosurvey in Queens, NYC after 1999 outbreak revealed $<1\%$ of infected individuals developed severe neurologic disease
- Much more likely to occur in elderly
 - Mean age of pts with severe neurologic dz (encephalitis/meningoencephalitis) in NY outbreak was 81.5
 - Age >75 yr correlated with poor prognosis

West Nile Encephalitis

- Sites of most common attack
 - Thalamus, midbrain, and brainstem (especially medulla per autopsy reports)
- Prognosis
 - Recovery nearly always complete
 - Residual weakness and memory loss typically clear up within a few weeks
 - Recovery more rapid in children
 - Fatality rates are 3% to 15%, mostly in the elderly or immunocompromised

West Nile Encephalitis - Diagnosis

- Laboratory findings
 - CSF (abnormalities may be minimal in a pure encephalitis):
 - Lymphocytic pleocytosis ($<100/\text{mm}^3$)
 - Increased protein concentration ($<150 \text{ mg/dL}$)
 - Normal glucose ($>50\%$ of blood value)
 - Leukopenia ($<4000/\text{mm}^3$ in 1/3 of pts)
- Radiology
 - CT or MRI can demonstrate presence and extent of inflammation in the brain

West Nile Encephalitis - Diagnosis

- Serology (CSF & Sera): WNV-specific IgM and IgG ELISAs
 - Preliminary screening for St Louis encephalitis may be done if WNV test not readily available
- Virus detection: PCR
 - Antigen-capture ELISAs may be used for virus detection in mosquito pools
- PCR is not as sensitive as serology

Treatment

- Mainly supportive at this time
 - Anti-pyretics
 - Seizure control with benzodiazepines (prophylaxis not recommended)
 - IV corticosteroids (i.e. dexamethasone) may be used to decrease inflammation (controversial)
 - Maintain elevation of the head
 - Monitor BP, O₂, and sodium levels

Treatment

- Consider immediate acyclovir in any patient with symptoms of encephalitis when etiology is unsure
- Ribavirin (an antiviral nucleoside analogue) is currently in human use for WNV
- Benefits from plasmapheresis in viral encephalitis are unclear

Other Complications

- Guillain-Barre Syndrome
- Myocarditis
- Pancreatitis
- Hepatitis
- These are more rare than encephalitis

Prevention and Control

- Mosquito control is the most effective means
- Mosquito abatement districts
 - Initiate larval control (larvicide) before disease transmission to human or domestic animals
 - Adult mosquito control (adulticide) within 2-mile radius of site of WNV-positive dead bird or infected mosquito pool

Surveillance

- Active bird surveillance
 - Wild birds (especially dead crows)
 - Sentinel birds (cooped chickens)
- Active mosquito surveillance
 - Early spring to late Oct in N.E., up to year-round in south
- Enhanced passive veterinary surveillance
 - Especially horses
- Enhanced passive human surveillance

NJDH Criteria for Diagnostic Testing for Suspected WNV

- Fever, Altered MS, CSF pleocytosis, +/- muscle weakness or flaccid paralysis
- Any presumptive dx of viral encephalitis
- Any case of Guillain-Barre or acute flacid paralysis
- Presumptive asceptic meningitis in county with confirmed WNV activity

Prevention and Control

- Fish (*Gambusia affinis*) are being used in waste water treatment plants in New York
- Bug Zappers are not effective
 - May actually spread viruses and bacteria
 - Not very effective at killing female mosquitoes
 - Effective at killing insects that prey on mosquitoes

Prevention and Control

- Public Outreach
 - Reduce breeding sites (collections of stagnant water) around the home
 - Decrease exposure risks
 - Avoid infested areas if possible
 - Wear long-sleeves and long pants
 - Use of insect repellants (i.e. DEET, Permethrin)

Future Directions

- Experimental inactivated vaccine in development
- Avian vaccine currently under study
- Pyrazofurin has demonstrated in vitro activity against WNV
- Dehydroepiandrosterone appears to promote survival in mice infected with WNV

